

10. An in vivo method of sealing air leaks in pulmonary tissues comprising the step of topically applying and curing the adhesive mixture of claims 1 to an air leak site in the pulmonary tissue.

11. An in vivo method to prevent post-surgical adhesions comprising the step of topically applying and curing the adhesive mixture of claims 1 to tissue surrounding a surgical site.

12. An in vivo method to seal tissue comprising the step of topically applying and bonding the adhesive mixture of claims 1 to tissue to prevent or control blood or other fluid leaks.

13. The adhesive composition of claim 1 wherein the second aqueous mixture is about 300–800 mg/ml of a crosslinking agent having a molecular weight in a range of about 5,000–15,000.

14. The adhesive composition of claim 13 wherein —LM— is a diester diradical of the formula $\text{—C(O)—(CH}_2\text{)}_2\text{—C(O)—}$.

15. The adhesive mixture of claim 1 wherein —LM— is a diester diradical of the formula, $\text{—C(O)—(CH}_2\text{)}_c\text{—C(O)—}$ where c is an integer from 2–10 and where the aliphatic portion of the diradical may be saturated or unsaturated.

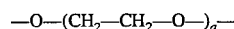
16. The adhesive composition of claim 15 wherein —LM— is an oligomeric diradical derived from polyglycolic acid.

17. A method of making a tissue adhesive consisting of the step of forming a mixture of

- i) a first aqueous mixture of about 20–60 wt/vol % serum albumin in about 0.01–0.25 molar buffer at a pH in a range of about 8.0–11.0,
- ii) a second aqueous mixture of about 50–800 mg/ml of a crosslinking agent having a molecular weight in a range of about 1,000–15,000, wherein the crosslinking agent is of the formula



wherein —PEG— is a diradical fragment represented by the formula



where a is an integer from 20–300;

wherein —LM— is a diradical fragment selected from the group consisting of a carbonate diradical of the formula, —C(O)— , a monoester diradical of the formula, $\text{—(CH}_2\text{)}_b\text{C(O)—}$ where b is an integer from 1–5, a diester diradical of the formula, $\text{—C(O)—(CH}_2\text{)}_c\text{—C(O)—}$ where c is an integer from 2–10 and where the aliphatic portion of the diradical may be saturated or unsaturated, a dicarbonate diradical of the formula $\text{—C(O)—O—(CH}_2\text{)}_d\text{—O—C(O)—}$ where d is an integer from 2–10, and an oligomeric diradical represented by the formulas —R—C(O)— , $\text{—R—C(O)—(CH}_2\text{)}_c\text{—C(O)—}$, or $\text{—R—C(O)—O—(CH}_2\text{)}_d\text{—O—C(O)—}$ where c is an integer from 2–10, d is an integer from 2–10, and R is a polymer or copolymer having 1–10 monomeric fragments selected from the group consisting of lactide, glycolide, trimethylene carbonate, caprolactone and p-dioxanone; and

wherein —G is a leaving group selected from the group consisting of succinimidyl, maleimidyl, phthalimidyl, imidazolyl, nitrophenyl or tresyl, and

wherein a combination of the first and second mixtures is initially liquid and then cures on the surface of tissue to give a flexible, substantive matrix which bonds to the tissue and has a burst strength greater than about 10 mmHg.

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